REPORT

The National Institute for Clinical Excellence (NICE)

A-T Rodgers

Ann Rheum Dis 2002;61(Suppl II):ii92–ii95

The National Institute for Clinical Excellence (NICE or the Institute) is part of the UK NHS. It provides guidance for the NHS and patients and their carers that aims to inform decisions about treatment and healthcare. Anne-Toni Rodgers, one of the directors of NICE and an executive lead for many NICE projects, provided an outline of the organisation and the Appraisal Process. In addition she summarised the Institute's recent guidance on the use of etanercept and infliximab for the treatment of rheumatoid arthritis.

BACKGROUND: NICE AND THE NHS

All healthcare workers want to give their patients the best possible care but they face two major problems.

- The rate of scientific and clinical discovery is so fast that it is hard for people to keep up to date with best practice.
- The demand for health care is greater than the resources (financial and human) available. This is attributable to past successes, the availability of effective new technologies, and the continued use of older, less effective technologies.

Every healthcare system in the world is struggling to find solutions to these problems. In Britain, as elsewhere, these problems have meant that healthcare professionals sometimes:

- started to use new treatments without adequate evidence of their clinical or cost effectiveness
- continued to use out of date treatments that have been replaced by newer developments
- have been too slow to introduce new treatments (even when they were shown to be clinically effective and value for money).

As a result, unacceptable variations in the quality of care available for patients were seen in different parts of the country (so called "postcode" prescribing). The white papers *The New NHS Modern and Dependable*¹ and *NHS Wales' Putting Patients First*,² set out the government's overall agenda for improving the quality of health care in the NHS

in England and Wales. More detail emerged in *A First Class Service: Quality in the New NHS*,³ which stated:

- "the objective is to ensure fair access to effective, prompt, high quality care wherever a patient is treated in the NHS"
- "we propose a new model which marries clinical judgment with clear national standards". The model described in *A First Class Service* (fig 1) sets out how this will be achieved, and the Institute's role. National standards will be available with local responsibility for their delivery and backed by consistent monitoring arrangements.

NICE ITSELF

From the reporting of NICE you would be forgiven for thinking that the Institute only provided guidance on the cost effectiveness of specific drugs. This is not the case, there are a number of strands to its work. Firstly, technology appraisals; NICE has completed 44 appraisals to date on topics as diverse as hip replacement joints, drugs for hyperactive children, and of course the use of etanercept and infliximab for the treatment of rheumatoid arthritis; and there are another 42 appraisals underway. Secondly, the national clinical guideline work programme—six clinical guidelines have been published to date, and 39 are under development, and thirdly NICE has recently taken over responsibility for the safety and efficacy of new interventional procedures. Finally, there are always ad hoc projects underway such as *Principles for Best Practice in Clinical Audit*,⁴ which NICE published with Radcliffe Medical Press earlier this year.

NICE AND THE REGULATORS

NICE is not a regulatory body and there is no link between a NICE appraisal and either the European or UK regulatory process. Regulators consider the safety and efficacy of a product and license it for sale, while NICE appraises the comparative evidence of clinical and cost effectiveness and suggests where the product can add value for the NHS and patients. While regulators license all products for sale, NICE only

Figure 1 NICE and the NHS.

Figure 2 The NICE Appraisal Process—in summary.

appraises around 30 technologies per year. NICE is asked to look at specific drugs and devices where the availability of the drug or device varies across England and Wales or where there is confusion or uncertainty over its value. Topics are selected by the Secretary of State for Health and the National Assembly for Wales. NICE is one of the organisations in Europe that looks at cost effectiveness as a part of its work. It is inevitable that there will be variations between countries when looking at clinical and cost effectiveness data—the price of the product can vary across Europe, as can the way health care is delivered (for example, insurance based provision, public provision). Although other countries may not have a single organisation with a work programme as diverse as the Institute's, they often require comparative data on both clinical and cost effectiveness after licensing and consider it carefully before deciding if the product is reimbursed by the public healthcare system. This is not only happening in Europe. In the USA, health management organisations (HMOs) have strict protocols for comparing new products against existing treatments that require evidence of clinical and cost effectiveness, and Australia and Canada have long established economic evaluation units.

TECHNOLOGY APPRAISALS: THE PEOPLE AND THE PROCESS

Appraisals are independent considerations of the clinical and cost effectiveness of health technologies. Topics include medicines, medical devices, diagnostic techniques, surgical/clinical procedures, and health promotion activities. NICE follows an open and transparent process⁵ for its appraisals (fig 2), which was developed after widespread consultation. It is advised by an independent Appraisal Committee and for each appraisal patient/carer and health professional organisations, nominate their own experts to help and inform the committee. The committee's members are drawn from the NHS, healthcare professionals working in the NHS, patients and carers, and the academic world and their details are published on the NICE web site. Although the Committee seeks the views of organisations representing healthcare professionals, patients and carers, manufacturers and the NHS, its advice is independent of any vested interests. Once a technology has been referred to NICE for appraisal, an independent academic centre is commissioned, through NHS Research and Development, to prepare an independent and systematic review of both the published evidence and any data submitted by manufacturers. This review is referred to as the Assessment Report. Stakeholders that will be involved in the appraisal are identified. They include national patient/carer organisations, healthcare professional bodies, and manufacturers related to the

technology and the condition it is indicated for, and representatives of NHS commissioning organisations (in England, Primary Care Trusts). Initially stakeholders are consulted on the list of other stakeholders and the scope of the appraisal. They are then invited to prepare written submissions, and nominate experts who provide both written and verbal evidence to the Appraisal Committee. All of the submissions, together with the Assessment Report and any comments on it received after stakeholder consultation, are combined to form an Evaluation Report that is sent to the Appraisal Committee and the Experts advising it. The Appraisal Committee meets to consider this report alongside the expert witnesses. After this meeting the Committee formally consult on their initial thoughts with all of the stakeholders. The consultation document is called an ACD (Appraisal Consultation Document). The ACD and Assessment Report are also published on the NICE web site where individuals can comment. This is a genuine consultation process—NICE is clear that the ACD does not constitute the Institute's guidance, and that any recommendations it makes are preliminary and may change after consultation. The Appraisal Committee then considers feedback from the formal consultees, the expert witnesses and those sending in comments via the web site. They draft a Final Appraisal Determination (FAD), which is sent to NICE. NICE considers the committee's recommendations, and to ensure that the final guidance it issues is robust sends the FAD to the same stakeholder groups who are provided with the opportunity to appeal.⁶ Appeals can be made if stakeholders consider that the guidance is perverse (based on the evidence base, which they see), that NICE has not followed the process properly, or if they believe NICE has exceeded its powers. If there are no appeals, or if appeals are heard but not upheld, then the FAD becomes guidance and NICE issues it directly to the NHS. If appeals are made then the Institute considers them carefully. If appeals are upheld NICE asks the independent advisory committee to look again at the evidence and their recommendations. On average each appraisal takes around 12 months to complete. Some appraisals take longer as they are extended to include important research, or to consider particular issues such as regulatory approvals. All guidance is reviewed, and the review date is set after consultation so that it coincides with any major new evidence.

NICE GUIDANCE

NICE has issued guidance on the use of etanercept for juvenile idiopathic arthritis⁶; the use of etanercept and infliximab for rheumatoid arthritis⁷; and the cyclo-oxygenase (Cox) II selective inhibitors for osteoarthritis and rheumatoid arthritis.⁸ In

Box 1 Documentation and opinion made available to the Appraisal Committee during the assessment of etanercept and infliximab for rheumatoid arthritis Assessment Report:

Prepared by West Midlands Development and Evaluation Service, The University of Birmingham (*The clinical effectiveness and cost effectiveness of new drug treatments for rheumatoid arthritis: etanercept and infliximab*), September 2001

Manufacturer/sponsor submissions:

- Schering-Plough
- Wyeth Laboratories

Professional/specialist group and patient group submissions from:

- Royal College of General Practitioners
- Chartered Society of Physiotherapy
- Institute for the Health of the Elderly
- British League Against Rheumatism (on behalf of Arthritis Care, Arthritis Research Campaign, British Health Professionals in Rheumatology, British Society for Rheumatology, Primary Care Rheumatology Society, and the Royal College of Nursing Rheumatology Policy and Practice Group)
- Department of Health

External expert and patient advocate submissions from:

- Dr Ernest Choy, Department of Rheumatology, King's College Hospital, London
- Dr Ian Griffiths, Consultant Rheumatologist, Freeman Hospital, Newcastle upon Tyne
- Neil Betteridge, Head of Public Policy and Campaigning, Arthritis Care

addition it has issued guidance on the use of metal on metal hip replacement,⁹ hip prosthesis for primary hip replacement,¹⁰ and autologous cartilage transplantation of full thickness cartilage defects in knee joints.¹¹ Copies of the guidance are available free of charge from the NICE web site (www.nice.org.uk). The guidance on the etanercept and infliximab for the treatment of rheumatoid arthritis was issued in March 2002. Development involved the health professionals, manufacturers, and patient and carer organisations listed in box 1. In summary the guidance states that:

- Etanercept and infliximab (infliximab only in combination with methotrexate) are recommended as options for adults with continuing clinically active rheumatoid arthritis who have not responded adequately to at least two disease modifying antirheumatic drugs, including methotrexate (unless contraindicated).
- Etanercept and infliximab should be prescribed in accordance with British Society of Rheumatology (BSR) guidelines April 2001,¹² criteria for eligibility, definitions of failure of standard treatment, exclusion criteria, and criteria for withdrawal of treatment. In particular, treatment should be withdrawn in the event of severe drug related toxicity or because of lack of response at three months.
- Prescription and follow up should be undertaken only by a consultant rheumatologist
- The choice of which of the two agents is used should be determined by consultation between the patient and the clinician responsible, taking into account differences in treatment schedules and patient preferences.
- Maintenance treatment with these agents in those who respond to treatment initially should be at the lowest licensed dose compatible with continuing clinical response.

Table 1 Appraisals to 28 June 2002

	Review of completed technology appraisals (06.06.02)			
	Total appraisals	Routine use	Selective use	Research only
All	44*	13	27	4
Pharmaceuticals	31 (72)	10	20	1
Devices	8 (80)	3	5	0
Diagnostics	1 (5)	0	0	1
Procedures	4 (12)	0	2	2
Health promotion	0	0	0	0

*Includes both appraisals of taxanes for breast cancer (figures in parentheses = number of topics).

- All clinicians prescribing etanercept or infliximab should (with the patient's consent) register the patient with the Biologics Registry established by the BSR and forward information on dose, outcome, and toxicity on a six monthly basis.
- There is currently no evidence to support treatment beyond four years. A decision to continue treatment should therefore be contingent on ongoing monitoring of disease activity and clinical effectiveness in individual cases. Outcomes from the BSR Biologics Registry will help inform such decisions.
- There is no evidence for the consecutive use of these agents, and therefore this is not recommended. Like all NICE guidance this guidance will be reviewed, the planned review date is set for March 2005

SUMMARY

NICE produces guidance describing where a technology is clinically and cost effective. The decision as to whether it is affordable, or whether it is desirable, is a matter for UK ministers. To date it is estimated that the appraisal guidance NICE has issued has potentially increased NHS spending by about £550 million, and thus promoted equitable access to those technologies that add value. Table 1 summarises these appraisals.

NICE is aware that the decisions it is asked to make are among the most difficult in public life. Both NICE and those forming its independent advisory committees, are acutely aware of the responsibility they carry and form their guidance with great care. The members of the independent committees who advise NICE deserve credit for the calm and considered way in which they analyse and interpret the evidence before them, notwithstanding the storms of publicity and promotion that sometimes surround the medicines they are asked to evaluate.

NICE is an open and transparent organisation, and all information regarding the processes it follows and the people involved can be found on the NICE web site. In addition the email notify option, provides those who register with the facility to receive automatic updates from the site.

.....

Author's affiliations

A-T Rodgers, National Institute for Clinical Excellence

Correspondence to: A-T Rodgers; anne-toni.rodgers@nice.nhs.uk

REFERENCES

- 1 *The New NHS: modern dependable*. Presented to Parliament by the Secretary of State for Health by Command of Her Majesty, December 1997.
- 2 *Putting patients first*. Presented to Parliament by the Secretary of State for Wales by command of Her Majesty, January 1998.
- 3 **Department of Health**. *A first class service—quality in the new NHS*. London: Department of Health, August 1998

- 4 **NICE.** *Principles for best practice in clinical audit.* Oxford: Radcliffe Medical Press, 2002.
- 5 **National Institute for Clinical Excellence.** *Guide to the technology appraisal process.* London: National Institute for Clinical Excellence, 2001. Available from www.nice.org.uk
- 6 **National Institute for Clinical Excellence.** *Guidance on the use of etanercept for juvenile idiopathic arthritis.* NICE Technology Appraisal Guidance no 35. London: National Institute for Clinical Excellence, 2002. Available from www.nice.org.uk
- 7 **National Institute for Clinical Excellence.** *Guidance on the use of etanercept and infliximab for rheumatoid arthritis.* NICE Technology Appraisal Guidance no 36. London: National Institute for Clinical Excellence, 2002. Available from www.nice.org.uk
- 8 **National Institute for Clinical Excellence.** *Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis.* NICE Technology Appraisal Guidance no 27. London: National Institute for Clinical Excellence 2001. Available from www.nice.org.uk
- 9 **National Institute for Clinical Excellence.** *Guidance on the use of metal on metal hip resurfacing arthroplasty.* NICE Technology Appraisal Guidance no 44. London: National Institute for Clinical Excellence, 2002. Available from www.nice.org.uk
- 10 **National Institute for Clinical Excellence.** *Guidance on the selection of prostheses for primary total hip replacement.* NICE Technology Appraisal Guidance no 2. London: National Institute for Clinical Excellence, 2000. Available from www.nice.org.uk
- 11 **National Institute for Clinical Excellence.** *Guidance on the use of autologous cartilage transplantation of full thickness cartilage defects in knee joints.* NICE Technology Appraisal Guidance no 16. London: National Institute for Clinical Excellence, 2000. Available from www.nice.org.uk
- 12 **The British Society of Rheumatology.** *Guidelines for prescribing TNF- α blockers in adults with rheumatoid arthritis.* London: British Society of Rheumatology, 2001. Available from www.rheumatology.org.uk